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Research article

Thermodynamic, kinetic and docking studies of some unsaturated fatty acids-quercetin derivatives as inhibitors of mushroom tyrosinase

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Abstract: Inhibition of activity and stability structure of mushroom tyrosinase (MT) is highly important, since it is a key enzyme of melanogenesis playing various roles in organisms. In this study, thermodynamic stability and diphenolase activities were investigated in the presence of quercetin-7-linoleate (ligand I) and quercetin-7-oleate (ligand II) on mushroom tyrosinase by experimental and computational methods. Kinetic analyses showed that the inhibition mechanism of these ligands is reversible and competitive manner. The inhibition constants values (K_{iI} = 0.31 and K_{iII} = 0.43 mM) and the half maximal inhibitory concentration (IC_{50} = 0.58 and 0.71 mM) were determined for ligand I and ligand II respectively. Thermal denaturation for the sole and modified enzyme were performed by using fluorescence spectroscopy to obtain the thermodynamic parameters of denaturation. Type of interactions and orientation of ligands were determined by molecular docking simulations. The binding affinities of the MT–ligand complexes during docking were calculated. In the computational studies performed using the MT (PDBID: 2Y9X) from which tropolone was removed, we showed that the ligands occupied different pockets in MT other than the active site. The best binding energies with values of −9 and −7.9 kcal/mol were calculated and the MolDock scores of the best poses with the lowest root mean square deviation (RMSD) were obtained as −172.70 and −165.75 kcal/mol for complexes of MT–ligand I and MT–ligand II, respectively. Computational simulations and experimental analysis demonstrated that the ligands increased the mushroom tyrosinase stability by reducing the activity of enzyme. In this regard, ligand I showed the potent inhibitory and played an important role in enzyme stability.